Safety and Immunogenicity of a Recombinant Adenovirus Serotype 35-Vectored HIV-1 Vaccine in Adenovirus Serotype 5 Seronegative and Seropositive Individuals.

Jonathan D Fuchs, San Francisco Department of Public Health
Pierre-Alexandre Bart, Centre Hospitalier Universitaire Vaudois
Nicole Frahm, Fred Hutchinson Cancer Research Center
Cecilia Morgan, Fred Hutchinson Cancer Research Center
Peter B Gilbert, Fred Hutchinson Cancer Research Center
Nidhi Kochar, Fred Hutchinson Cancer Research Center
Stephen C DeRosa, Fred Hutchinson Cancer Research Center
Georgia D Tomaras, Duke University
Theresa M Wagner, San Francisco Department of Public Health
Lindsey R Baden, Brigham and Women’s Hospital

Only first 10 authors above; see publication for full author list.

Journal Title: Journal of AIDS and Clinical Research
Volume: Volume 6, Number 5
Publisher: OMICS International | 2015-05-23, Pages 461-None
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.4172/2155-6113.1000461
Permanent URL: https://pid.emory.edu/ark:/25593/r9g92

Final published version: http://dx.doi.org/10.4172/2155-6113.1000461

Copyright information:
©2015 Fuchs JD, et al.
This is an Open Access work distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/).

Accessed November 12, 2017 8:34 PM EST
Safety and Immunogenicity of a Recombinant Adenovirus Serotype 35-Vectored HIV-1 Vaccine in Adenovirus Serotype 5 Seronegative and Seropositive Individuals


1Population Health Division, San Francisco Department of Public Health, San Francisco, CA, USA
2Department of Medicine, University of California, San Francisco, San Francisco, USA
3Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland
4Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA
5Human Vaccine Institute, Duke University, Durham, NC, USA
6Division of Infectious Disease Prevention, Brigham and Women’s Hospital, Boston, MA, USA
7Laboratory of Infectious Disease Prevention, New York Blood Center, New York, NY, USA
8The Hope Clinic, Division of Infectious Diseases, Emory University, Atlanta, GA, USA
9Infectious Diseases Division, Vanderbilt University School of Medicine, Nashville, TN, USA
10University of Rochester School of Medicine and Dentistry, Rochester, New York, NY USA
11Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA
12Infectious Diseases Division, Columbia University College of Physicians and Surgeons, New York, NY, USA
13Fenway Health and the Division of Infectious Diseases, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, USA
14Division of AIDS, National Institute of Allergy and Infectious Diseases, Bethesda, MD, USA
15Vaccine Research Center, National Institute of Allergy and Infectious Diseases, Bethesda, MD, USA

Abstract

Background: Recombinant adenovirus serotype 5 (rAd5)-vected HIV-1 vaccines have not prevented HIV-1 infection or disease and pre-existing Ad5 neutralizing antibodies may limit the clinical utility of Ad5 vectors globally. Using a rare Ad serotype vector, such as Ad35, may circumvent these issues, but there are few data on the safety and immunogenicity of rAd35 directly compared to rAd5 following human vaccination.

Methods: HVTN 077 randomized 192 healthy, HIV-uninfected participants into one of four HIV-1 vaccine/placebo groups: rAd35/rAd5, DNA/rAd5, and DNA/rAd35 in Ad5-seronegative persons; and DNA/rAd35 in Ad5-seropositive persons. All vaccines encoded the HIV-1 EnvA antigen. Antibody and T-cell responses were measured 4 weeks post boost immunization.

Results: All vaccines were generally well tolerated and similarly immunogenic. As compared to rAd5, rAd35 was equally potent in boosting HIV-1-specific humoral and cellular immunity and responses were not significantly attenuated in those with baseline Ad5 seropositivity. Like DNA, rAd35 efficiently primed rAd5 boosting. All vaccine regimens tested elicited cross-clade antibody responses, including Env V1/V2-specific IgG responses.

Conclusions: Vaccine antigen delivery by rAd35 is well-tolerated and immunogenic as a prime to rAd5 immunization and as a boost to prior DNA immunization with the homologous insert. Further development of rAd35-vected prime-boost vaccine regimens is warranted.

Keywords: HIV Vaccine; Adenovirus 35; Adenovirus 5; DNA vaccine; Randomized clinical trial

Introduction

The development of a safe and effective preventive HIV vaccine remains an urgent public health priority in the setting of an estimated 2.1 million new infections globally [1]. Since the first preventive HIV vaccine candidate entered clinical testing in 1987, four distinct vaccine concepts including subunit protein, DNA, and viral vector vaccines have been evaluated in six completed efficacy trials [2-7]. Thus far, only one vaccine regimen, a canarypox vector encoding three HIV-1 genes with a gp120 subunit boost, demonstrated partial efficacy in a phase 2b study [6]. Subsequent findings indicated that non-neutralizing IgG antibody responses to HIV-1 Env V1/V2 were significantly correlated with decreased risk of infection in vaccines [8].

HIV vaccine candidates using recombinant adenovirus (rAd) vectors have been some of the most immunogenic [9]. The Step study (HIV Vaccine Trials Network [HVTN] 502) was the first efficacy trial to test an rAd5-vected vaccine expressing HIV-1 clade B Gag, Pol and Nef; however the product failed to protect against infection or disease progression. Furthermore, this study suggested that pre-existing Ad5 neutralizing antibodies may have played a role in increased HIV susceptibility among vaccines [4,10]. A multiclade/multigene DNA prime, rAd5 boost regimen encoding HIV-1 Gag, Pol, and Nef from the Hope Clinic, Div of Infectious Diseases, Emory University, Atlanta, GA, USA

*Corresponding author: Jonathan D Fuchs, San Francisco Department of Public Health, 25 Van Ness Ave, Suite 100, San Francisco, CA, 94102, USA, Tel: 01 415 336-1290; E-mail: jonathan.fuchs@sfdph.org

Received April 09, 2015; Accepted May 12, 2015; Published May 23, 2015


Copyright: © 2015 Fuchs JD, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
The adenovirus 5 (Ad5) neutralizing antibody (nAb) ≥ 18 represents Ad5 seropositive individuals; ‘N’ represents the active vaccine/placebo recipients who were blinded to treatment assignment within each treatment group. DNA vaccinations were delivered by Biojector, and adenovectors were delivered by needle and syringe. Groups 2 and 3 were blinded to assignment to these groups.

Table 1: HVTN 077 Protocol Schema.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Ad5 nAb*</th>
<th>N**</th>
<th>Injection schedule months (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 (0)</td>
<td>1 (28)</td>
<td>2 (56)</td>
</tr>
<tr>
<td>1</td>
<td>&lt;18</td>
<td>34/6</td>
<td>rAd5</td>
</tr>
<tr>
<td>2</td>
<td>&lt;18</td>
<td>48/8</td>
<td>DNA</td>
</tr>
<tr>
<td>3</td>
<td>&lt;18</td>
<td>48/8</td>
<td>DNA</td>
</tr>
<tr>
<td>4</td>
<td>≥18</td>
<td>34/6</td>
<td>DNA</td>
</tr>
<tr>
<td>Total</td>
<td>192</td>
<td>164/2</td>
<td>-</td>
</tr>
</tbody>
</table>

*Adenovirus 5 (Ad5) neutralizing antibody (nAb) ≥ 18 represents Ad5 seropositive individuals; **N represents the active vaccine/placebo recipients who were blinded to treatment assignment within each treatment group. DNA vaccinations were delivered by Biojector, and adenovectors were delivered by needle and syringe. Groups 2 and 3 were blinded to assignment to these groups.

HIV-1 Envelope-specific IgG to Group M Consensus (Con S gp140 CF1), Clade A (00MSA gp140), Clade B (B.con.env03 140 CF), and Clade C (C.con.env03 140 CF) were performed according to a pre-defined assay study plan following GCLP guidelines. Additional studies were performed for Env V1V2 reactive antibodies [8] utilizing scaffolds gp70 V1V2 VRC EnvA [27] and gp70 V1V2 (Case A2) [28]. HIV-1-specific IgG was detected from 1:50 serum dilution with biotin-conjugated mouse anti-human IgG (Southern Biotech, Birmingham, AL) (4 µg/ml), followed by washing and incubation with streptavidin-PE (BD Pharmingen). Mean fluorescent intensity (MFI) readouts were acquired on a Bio-Plex instrument (BioRad). Positive controls (purified HIV-1 positive immunoglobulin [HIVIG] and CH58 mAb [27] for the V1V2 assays) and negative controls (blank beads, HIV-1 negative sample, and baseline samples) were included to ensure specificity and for maintaining consistency and reproducibility between assays.

Positivity of antibody binding at Day 196 was defined by meeting all three conditions: (1) the MFI minus blank values are ≥ 2-antigen-specific cutoff (based on the average + 3 standard deviations of 80 seronegative plasma samples), (2) the MFI minus blank values are greater than 3 times the baseline (Day 0) MFI minus blank values, and (3) the MFI values are greater than three times the baseline MFI values. For positive responses, binding magnitude was quantified by the net MFI concentration (subtracting the blank value) estimated using a 10-point standard curve (4 PfU).

T Cell Response: Peripheral blood mononuclear cells (PBMC) were isolated and cryopreserved from whole blood within 8 hours of venipuncture using standard procedures [29]. A 10-color intracellular cytokine staining (ICS) assay was performed on cryopreserved PBMC as previously described [30-32]. For the detection of HIV-specific T cells, thawed PBMC were rested overnight and then stimulated for 6 hours with overlapping HIV-1 15-mer peptide pools matched to the vaccine insert (VRC EnvA). Positivity was established at p<0.001 using a Fisher’s exact test comparing stimulated and unstimulated samples.

Statistical analysis

All data from enrolled participants who received at least one vaccination were analyzed. Five study groups were evaluated for immunogenicity: the four vaccinated groups individually plus the pooled placebo group. HIV-1 specific IgG binding antibody and T-cell responses were evaluated at baseline (Day 0, IgG only) and at the primary immunogenicity timepoint, Day 196 (one month after the final injection). Rates of HIV-1 Env-specific antibodies and positive CD4+ and CD8+ T-cell responses (for cells expressing IFN-γ and/or IL-2 as measured by ICS) were estimated for each study group and timepoint. Lachenbruch’s test was used for comparing primary immunogenicity endpoints between study groups [33]. Response rates were compared between groups using Fisher’s exact tests. Magnitudes of responses among positive responders were compared between study groups using Wilcoxon rank sum tests. All statistical tests were 2-sided. Primary and secondary analyses comparing immunogenicity endpoints between vaccinated groups were considered statistically significant if p ≤ 0.033, chosen to control the overall type I error rate at 0.10 and correcting for three pairwise comparisons. All other analyses used p ≤ 0.05 to judge statistical significance. All descriptive and inferential statistical analyses were performed using SAS and/or R statistical software.

Results

Participant accrual, demographic data, and vaccine safety

Of the 736 individuals who underwent screening procedures, 40.3% had detectable neutralizing antibodies to Ad5 whereas only 9% were Ad35 seropositive (Table 2). The median age of the 192 enrolled participants was 28 years; 42% were women, 65% were non-Hispanic whites, 8% were Hispanic, and 16% Non-Hispanic Black. All participants received their initial vaccination and 98% received the second vaccination; of those assigned to 4 injections, 94% received the third, and 90% all four vaccinations. No significant differences were observed in vaccine completion rates between treatment groups. The primary reasons for study discontinuation included loss to follow-up or participant relocation (n= 9), incarceration (n=1), refusal (n=2) or other reasons (n=2); none were due to adverse experiences or reactogenicity related to vaccination.

Overall, each of the vaccine components was well tolerated. Pain or tenderness at the injection site was reported most commonly (88% of study participants). Differences between groups were detected; as seen in Figure 1, those receiving the rAd35/rAd5 heterologous adenovector regimen were less likely to report local reactions compared to the DNA prime, adenovector boost regimens (p<0.001). Maximum systemic symptoms were less commonly reported by those with pre-existing neutralizing antibodies to Ad5 (T4, Figure 1). There were 22 adverse events that were at least probably or definitely attributed to the vaccine, and most were local injection site reactions that were characterized as mild or moderate in severity. One case of transient mild leukopenia deemed probably related to vaccination was observed after receiving DNA in a T4 participant. Four expedited adverse events were reported in the trial including rectal bleeding, post traumatic lower extremity and right intraorbital ethmoid fractures, bipolar disorder, and gallstone pancreatitis; none were attributed to product. No significant differences in laboratory parameters were noted among groups. Overall, 60% had evidence of vaccine-induced HIV seroreactivity at the end of study using several commercially available HIV test kits. Rates were highest among rAd35/rAd5 vaccinees (81.8%) and lowest among participants who received DNA/rAd5 (45.7%).

HIV-1-specific antibody responses

Each of the vaccine regimens induced high frequency and magnitude cross-clade binding antibody responses (Figure 2). The antibody response rates were 100% for all treatment groups recognizing the consensus M gp140 (data not shown) and 97-100% recognizing the clade A Env antigen. For the clade B antigen, responses were also detected in greater than 92% of individuals. For the clade C antigen, response frequencies were highest for rAd35/rAd5 (96%) compared to the DNA prime/adenovector boost groups (76-78% for groups 2-4), however at lower magnitude in comparison to the DNA/rAd5 group (p=0.02).

Based on evidence that IgG binding antibodies to V1/V2 were correlated with reduced risk of HIV infection in the RV144 vaccine...
Figure 1: Safety assessment, showing maximum local reactogenicity A) and systemic reactogenicity, B) by treatment group. Subjects in control (C) groups 1-4 received group phosphate buffered saline. Subjects in treatment groups 1-3 (T1-T3) were Ad5 seronegative at baseline and received: T1- recombinant Ad35 (rAd35) prime and rAd5 boost; T2- three DNA priming injections boosted by rAd5; and T3- three DNA priming injections boosted by rAd35. Subjects in T4 were Ad5 seropositive at baseline and received three DNA priming injections boosted by rAd35. P values for comparisons of local and systemic reactogenicity were determined using the Kruskal-Wallis test.
Figure 2: Binding antibody net responses to Clades A (OOMSA 4076 gp140), B (B.con.env03 140CF), and C (C.con.env03 140CF) isolates 4 weeks after the boost vaccination as measured by median fluorescence intensity (MFI)-Blank where ‘Blank’ is a sample specific background measure. Responders are shown in red circles and non-responders in blue triangles. Box plots display the distribution of positive responses for the vaccinees for each antigen. P-values are derived from Lachenbruch’s test comparing rAd5 and rAd35 boosted groups in Ad5 seronegative individuals and the Ad35-boosted group in Ad5 seropositive individuals.
We explored whether the EnvA constructs tested in the HVTN 077 elicited these responses. Among positive responders, all treatment groups elicited gp70V1/V2 responses using the V1/V2 scaffold tested in the RV144 study (Case A2, Figure 3A) and there were no significant differences by group in the magnitude or frequency of the responses. In addition, we looked at the matching clade A V1/V2 sequence in the HVTN 077 vaccine regimen (clade A gp70V1/V2). Although the frequency of response did not differ substantially by group, as seen in Figure 3B, the response magnitude for binding antibodies to the vaccine-matched clade A gp70V1/V2 was significantly higher among the DNA/rAd5 group compared to the rAd35/rAd5 group, (p=0.005).

**HIV-1–specific T-cell responses**

As seen in Figure 4, HIV-1-specific T cells producing IFN-γ and/or IL-2 in response to vaccine insert-matched peptides were detected readily in each of the treatment groups. With regard to the CD4+ T-cell responses, the highest post-boost response rates were seen among Ad5 seronegative individuals receiving DNA/rAd35 (25/36, 69.4%) and lowest among those receiving rAd35/rAd5 (9/24, 37.5%); responses did not differ significantly across groups. Vaccine-induced CD8+ T-cell responses were elicited most frequently among Ad5 seronegative individuals who received the DNA/rAd5 regimen (32/42, 76.2%) and least among Ad5 seropositives who received the DNA/rAd35 regimen (10/25, 40.0%); responses did not differ significantly across groups. Overall, we found that among Ad5 seronegative subjects, 15%, 39%, and 32% of rAd35/rAd5, DNA/rAd5, and DNA/rAd35 recipients, respectively, and 14% of Ad5 seropositive participants receiving the DNA/rAd5 regimen developed both CD4+ and CD8+ T-cell responses. The HIV-specific CD4+ or CD8+ T-cell response magnitudes for positive responders after boosting were similar across groups.

In addition, we assessed expression of TNF-α and Granzyme B (GzB) in response to stimulation with insert-matched peptides. As shown in Figure 5, priming with DNA followed by either rAd35 or rAd5 led to the induction of significantly more polyfunctional CD4+ T cells than vaccination with rAd35/rAd5 in Ad5 seronegative subjects (p=0.0005 for three and p=0.007 for four functions, respectively, comparing the combined DNA/rAd5 and DNA/rAd35 groups with rAd35/rAd5 for Ad5 seronegative subjects). Interestingly, the patterns of combined expression of these functional markers did not differ significantly across groups.
Figure 4. HIV-specific CD4+ and CD8+ T-cell responses: The percentage of CD4+ (panel A) and CD8+ (panel B) T cells producing γ-interferon (IFN-γ) and/or interleukin-2 (IL-2) in response to EnvA matched peptide pools 4 weeks after the priming immunization(s) and 4 weeks after the boost as measured by intracellular cytokine staining. Responders are shown in red circles and non-responders in blue triangles. Boxplots show the distribution of the magnitude of response in positive responders only. The box indicates the median and interquartile range (IQR); whiskers extend to the furthest point within 1.5 times the IQR from the upper or lower quartile. Numbers at the top of each panel show the number of responders / number with an assay result and the percent with positive response. P-values are derived from Lachenbruch’s test comparing rAd5 and rAd35 boosted groups in Ad5 seronegative individuals and the Ad35-boosted group in Ad5 seropositive individuals. Data from samples with high background cytokine secretion was filtered, leading to differences in the number of samples with available data for CD4+ and CD8+ T cells.
differ significantly between these groups after correction for multiple comparisons (Supplementary Figure 1). While around 90% of HIV-specific CD8+ T cells were polyfunctional (Figure 5), only minor differences in expression patterns were observed among the different groups (Figure 5 and Supplementary Figure 1).

**Discussion**

In this clinical study of a prototype rAd35 vectored HIV-1 vaccine, we found that it was well tolerated with a similar safety profile to that of rAd5-based experimental vaccines [12,34]. We sought to explore how the immunogenicity of the heterologous rAd35/ rAd5 regimen compared to a DNA/rAd5 regimen, and found that rAd35/rAd5 elicited similar frequency and magnitude of HIV-1–specific antibody responses, and slightly (although not statistically significant) lower T cell responses. In addition, we found that as a boost in DNA-primed subjects, there were no significant differences between rAd35 and rAd5 in the ability to induce EnvA-specific antibody and T-cell responses. We also observed that in the setting of pre-existing Ad5 nAbs, there was no significant reduction of HIV-1 specific antibody or cellular responses to an Ad35-based regimen when given once as a boost. This confirms findings from preclinical models that cross-reactive immune responses from these serologically distinct adenoviruses are unable to substantially dampen immunogenicity [23]. Finally, we found that each of the vaccine regimens tested in this trial was capable of inducing cross-clade binding antibodies as well as V1/V2-specific IgG antibodies, which were correlated with reduced risk of HIV infection in the RV144 vaccine efficacy trial [8].

The HVTN 505 Phase Ib efficacy trial showed that a DNA/rAd5 prime-boost regimen encoding EnvA, EnvB, EnvC, clade B Gag, Pol, and Nef was unable to prevent HIV acquisition or reduce viral load [7]. Of note, in HVTN 077, we found the proportion of vaccinees with V1/V2 IgG responses (52% to 66% across the four groups) was similar to the rate observed for the partially efficacious ALVAC/gp120 vaccine regimen tested in the RV144 trial (64%, 95% CI 58% to 70%) [8] and higher than the 17.5% rate of response elicited by the HVTN 505 regimen [7]. In addition, the V1/V2 IgG responses were similar between groups 2 and 3 (DNA/rAd5 and DNA/Ad35 in Ad5 seronegative subjects), and group 4 (DNA/rAd35 in Ad5 seropositive subjects). This is in contrast to findings from the phase 2 study of the VRC multiclade DNA/rAd5 regimen [12], where V1/V2 IgG responses were significantly lower in Ad5 seropositive vaccines compared to Ad5 seronegative individuals (G. Tomaras, personal communication). These findings suggest that presentation of the EnvA antigen alone may produce a more favorable antibody response to the V1/V2 region than presentation of multiple Env proteins with additional competing antigens. It is important to note that we do not know if the V1/V2 IgG correlate of risk translates into a correlate of protection, and, if so, whether it is a mechanistic or non-mechanistic correlate [35] or whether IgG V1/V2 responses will be a correlate of HIV-1 risk or protection for vaccines in other populations that differ from the community-based sample evaluated in Thailand [6]. However, studies in non-human primate models suggest that envelope binding antibodies, V2-specific antibodies, and the avidity to which anti-Env antibodies bind to native trimer [18,36-38] can correlate with protection. Therefore, future HIV-1 vaccines designed to elicit Env binding responses and V2-specific IgG antibodies, should consider these observations from preclinical studies and recent clinical trials.

Whether multi-dose DNA priming for an adenovector boost confers an immunologic advantage over heterologous adenovector regimens is relevant given the desire for less complex vaccine regimens with fewer required immunizations. Compared to rAd35/rAd5, we found that the DNA/rAd5 regimen elicited higher magnitude binding antibody responses to some of the antigens tested (e.g., the EnvA clade-matched V1/V2 expressed by the vaccine and EnvC) but not to others (e.g., the Clade A Env). And while there was no overall difference in the HIV-specific CD4+ or CD8+ T-cell responses elicited by these regimens, DNA priming may generate more polyfunctional responses than the heterologous adenovector prime-boost regimen, a desirable feature of vaccines designed to elicit cellular immunity [39,40]. Several studies in the field will provide further insights into the relative immunogenicity of prime-boost regimens combining different adenovectors such as...
Ad35 and Ad26 encoding an EnvA antigen (IAVI B003-IPCAVD004-HVTN091, NCT01215149) and DNA administered by electroporation with a multi-antigen rAd35 construct (IAVI004; NCT01496989). Furthermore, to optimize immunogenicity, trials should carefully consider the administration interval between adenovector prime and boost. Our study delivered rAd35 and rAd5 6 months apart, eliciting higher magnitude HIV-specific T-cell responses compared to rAd35/rAd5 given only 3 months apart in VRC’012 (NCT00479999) [22].

Conclusion
In this phase 1b study, we have demonstrated that rAd35 is well tolerated and immunogenic as a boost, is as potent as rAd5 in DNA primed individuals. In addition, the humoral and cellular responses elicited by rAd35 boosting are better preserved in the setting of pre-existing Ad5 seropositivity than responses to rAd5 boosting, suggesting that rAd35 is a reasonable choice for an alternative adenovector vaccine vector to diminish the impact of antivector immunity. Therefore, as additional safety data emerge from studies exploring alternative adenovector vectors in different global contexts, rAd35 should be considered for use as a vaccine delivery vector, particularly as effective antigen designs become available. This is particularly relevant when CD8+ T cell-mediated immunity is desirable in addition to antibody-based immunity, in subjects already primed with the antigens expressed by the rAd35 vector, and in settings with a high prevalence of pre-existing immunity to Ad5, such as in sub-Saharan Africa.

Acknowledgments
The authors would like to thank Drs. Denny Kim, Marcel Curlin, and Chuen-Yen Lau for their involvement in early study implementation, Dr. Gary Nabel for access to reagents to probe V1V2 antibody responses, and Stephen Voght for his assistance with preparation of the tables and figures herein. They would also like to acknowledge the contributions of the HVTN 077 study staff, the sites’ community advisory boards, and the clinical trial participants.

Author contributions
Designed the study: JF, PAB, PG, NF, SD, TW, BG*, MJM. Oversaw study conduct and managed participants at study sites: JF, PAB, LB, BK, MS, KM, PG, NR, SK, MK, MJM. Medical monitoring and study oversight: JF, PAB, ES*, CM, BG*. Oversaw performing immunogenicity assays and result interpretation: JF, NF, SD, SR, GT, JM, BG*. Analyzed the data: JF, NK, PG, NF, GT, BG*, MJM. Wrote the manuscript: JF, PG, NF, GT, BG, MJM.

*This paper was written by authors in their capacity as NIH employees, but the views expressed in this paper do not represent those of the NIH.

Financial Support
HVTN 077 was conducted by the HIV Vaccine Trials Network (HVTN) and supported by the National Institutes of Allergy and Infectious Diseases (NIAID-NIH). This work was also supported by the following grants: UM1 AI086614 (HVTN Core FHCR), UM1 A086835 (SCHARP), UM1 A086818 (HVTN Laboratory Program), UM1 A096452 (UAB), UM1A096418 (Emory), UM1A096511 (Rochester), UM1 A096942 (BWH and Fenway), UM1 A096470 (NY Blood Center—Bronx, NY Blood Center—Union Square and Columbia University), UM1 A096439 (Vanderbilt), UM1 A096496 (SFDPH), and UM1 A096481 (Seattle).

Clinical trials Registration. NCT00801697

References


Submit your next manuscript and get advantages of OMICS Group submissions

Unique features:
• User friendly/feasible website-translation of your paper to 50 world’s leading languages
• Audio Version of published paper
• Digital articles to share and explore

Special features:
• 400 Open Access Journals
• 30,000 editorial team
• 21 days rapid review process
• Quality and quick editorial, review and publication processing
• Indexing at PubMed (partial), Scopus, EI&CO, Index Copernicus and Google Scholar etc
• Sharing Option: Social Networking Enabled
• Authors, Reviewers and Editors rewarded with online Scientific Credits
• Better discount for your subsequent articles

Submit your manuscript at: http://www.omicsonline.org/submission